FILE 'USPAT' ENTERED AT 15:56:03 ON 09 OCT 1998

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**********************************
*      WELCOME TO THE            *
*   U.S. PATENT TEXT FILE        *
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=> e summers, nee/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	SUMMERS, MICHAEL E/IN
E2	USPAT	1	SUMMERS, MICHAEL P/IN
E3	USPAT	0	--> SUMMERS, NEE/IN
E4	USPAT	5	SUMMERS, NEIL/IN
E5	USPAT	1	SUMMERS, PATRICIA E/IN
E6	USPAT	1	SUMMERS, PATRICK D/IN
E7	USPAT	1	SUMMERS, PAUL E/IN
E8	USPAT	1	SUMMERS, PETER/IN
E9	USPAT	1	SUMMERS, PHILLIP M/IN
E10	USPAT	3	SUMMERS, RICHARD/IN
E11	USPAT	1	SUMMERS, RICHARD J/IN
E12	USPAT	1	SUMMERS, RICHARD JAY/IN

=> e mcwherter, ch/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	MCWETHY, WILLIAM H JR/IN
E2	USPAT	1	MCWHA, KEITH/IN
E3	USPAT	0	--> MCWHERTER, CH/IN
E4	USPAT	1	MCWHERTER, CHARLES A/IN
E5	USPAT	5	MCWHERTER, DAVID/IN
E6	USPAT	1	MCWHINNEY, JOSEPH/IN
E7	USPAT	2	MCWHINNEY, JOSEPH P/IN
E8	USPAT	1	MCWHINNIE, DAVID A JR/IN
E9	USPAT	1	MCWHINNIE, GEORGE G/IN
E10	USPAT	3	MCWHINNIE, JOHN/IN
E11	USPAT	1	MCWHINNIE, ROBERT/IN
E12	USPAT	1	MCWHINNIE, WILLIAM R/IN

=> s e4;d cit ab

L1 1 "MCWHERTER, CHARLES A"/IN

1. 4,829,052, May 9, 1989, Serine protease inhibitors; George I. Glover, et al., 514/12; 530/324; 930/250, DIG.821 [IMAGE AVAILABLE]

US PAT NO: 4,829,052 [IMAGE AVAILABLE] L1: 1 of 1

ABSTRACT:
Synthetic polypeptides are disclosed which exhibit potent serine protease inhibition. Methods and compositions useful for treating conditions caused by unwanted serine protease activity are also disclosed.

=> e feng, yiq/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	FENG, YINGDUO/IN
E2	USPAT	1	FENG, YINGJIE/IN
E3	USPAT	0	--> FENG, YIQ/IN
E4	USPAT	1	FENG, YOU CHING/IN
E5	USPAT	2	FENG, YU/IN
E6	USPAT	1	FENG, YUN/IN
E7	USPAT	3	FENG, YUSHU/IN
E8	USPAT	1	FENG, ZHEN/IN
E9	USPAT	1	FENG, ZHU/IN
E10	USPAT	2	FENG, ZIXIA/IN
E11	USPAT	1	FENGBAI, TAO/IN
E12	USPAT	1	FENGELLY, RAYMOND S/IN

=> e feng, yi/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	3	FENG, YEE C/IN
E2	USPAT	8	FENG, YEE CHANG/IN
E3	USPAT	3	--> FENG, YI/IN
E4	USPAT	1	FENG, YINGDUO/IN
E5	USPAT	1	FENG, YINGJIE/IN
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=> s epo or erythropoietin

4837 EPO
1324 ERYTHROPOIETIN
L2 5812 EPO OR ERYTHROPOIETIN

=> s circ? permut?

TERM 'CIRC?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

=> s circul? permut?

557067 CIRCUL?
7899 PERMUT?
L3 128 CIRCUL? PERMUT?
(CIRCUL?(W)PERMUT?)

=> s l2 and l3

L4 2 L2 AND L3

=> d 1-2

1. 5,766,945, Jun. 16, 1998, 10A1 Retroviral packaging cells and uses thereof; A. Dusty Miller, 435/235.1, 320.1, 325 [IMAGE AVAILABLE]

2. 5,635,599, Jun. 3, 1997, Fusion proteins comprising **circularly** **permuted** ligands; Ira H. Pastan, et al., 530/351; 435/69.1, 69.5, 69.52, 69.7; 530/350 [IMAGE AVAILABLE]

=> d 2 kwic

US PAT NO: 5,635,599 [IMAGE AVAILABLE] L4: 2 of 2
TITLE: Fusion proteins comprising **circularly** **permuted** ligands

ABSTRACT:
The present invention provides for **circularly** **permuted** ligands which possess specificity and binding affinity comparable to or greater than the specificity and binding affinity of the original (unpermuted) ligand. The invention further provides for novel fusion proteins comprising a **circularly** **permuted** ligand fused to one or more proteins of interest.

SUMMARY:

BSUM(1)

This invention relates to the production and use of **circularly** **permuted** ligands and fusions of two or more proteins where one of the proteins is **circularly** **permuted**.

SUMMARY:

BSUM(9)

This . . . desirability of such molecules was apparent prior to the work described here. Such rearranged molecules are also referred to as **circularly** **permuted** proteins.

SUMMARY:

BSUM(10)

The **circularly** **permuted** ligands are especially useful when employed as a component in a fusion protein of interest. Oftentimes fusion of a protein. . . to its receptor. Binding affinity of IL4 fusion proteins is greatly enhanced by the use of fusion proteins employing the **circularly** **permuted** IL4 molecules described here. It is believed that the reduced affinity in growth factor-toxin or other ligand-toxin fusion proteins is. . . have a binding specificity and affinity comparable to or greater than native ligand fusion proteins. Thus, a valuable use for **circularly** **permuted** ligands is disclosed here and it is shown that such functional permuted ligands may be effectively fused to proteins of. . .

DRAWING DESC:

DRWD(2)

FIG. 1 schematically illustrates the **circular** **permutation** of a linear polymer (e.g., a protein). (A) An unpermuted (native) linear protein of length J in which the amino. . .

DRAWING DESC:

DRWD(3)

FIG. 2 shows a schematic three dimensional diagram of IL4 and **circularly** **permuted** mutants. The three dimensional structure of IL4, based on the NMR coordinates (Powers et al. Science, 256: 1673-1677 (1992); Powers. . .

DRAWING DESC:

DRWD(4)

FIG. 3 shows the binding and proliferative activity of **circularly** **permuted** IL4 mutants. (A) Displacement analysis: Bound [.sup.125 I]-IL4 plotted as a function of IL4 (O), IL4(38-37) (.tangle-solidup.) or IL4(105-104) (.quadrature.). . .

DRAWING DESC:

DRWD(5)

FIG. 4 shows the binding and cytotoxic activity of **circularly** **permuted** IL4-PE fusion protein IL4(38-37)-PE38QQRDEL compared to the native IL4-PE fusion protein IL4-PE38QQRDEL. (A) Amount of ([.sup.125 I]-IL4) bound to DAUDI. . .

DETDESC:

DETD(3)

The term "**circularly** **permuted**" as used herein refers to a linear molecule in which the termini have been joined together, either directly or through. . . opened at another location to produce a new linear molecule with termini different from the termini in the original molecule. **Circular** **permutations** include those molecules whose structure is equivalent to a molecule that has been circularized and then opened. Thus, a **circularly** **permuted** molecule may be synthesized de novo as a linear molecule and never go through a circularization and opening step. The particular **circular** **permutation** of a molecule is designated by brackets containing the amino acid residues between which the peptide bond is eliminated. Thus, the designation IL4(105-104) designates a **circularly** **permuted** IL4 growth factor in which the opening site (position at which the peptide bond is eliminated) occurred between residues 105. . .

DETDESC:

<------User Break------>
u

The . . . used herein to provide a reference point for the ligand, growth factor or protein prior to its rearrangement into a **circularly** **permuted** molecule, as described above. Typically, the unmodified ligand, growth factor or protein has amino and carboxyl termini and an
=> d 1-2e pastan, i/in

'I' MUST END IN '/Q', '/A', OR '/L'

=> e pastan, i/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	PASTAN, HARVEY/IN
E2	USPAT	6	PASTAN, HARVEY L/IN
E3	USPAT	0 -->	PASTAN, I/IN
E4	USPAT	19	PASTAN, IRA/IN
E5	USPAT	9	PASTAN, IRA H/IN
E6	USPAT	1	PASTAN, IRA HARRY/IN
E7	USPAT	1	PASTARI, GUENTER/IN
E8	USPAT	1	PASTARI, GUNTHER/IN
E9	USPAT	1	PASTCHETT, ARTHUR A/IN
E10	USPAT	2	PASTECKI, ANDREW S/IN
E11	USPAT	4	PASTECKI, PETER A/IN
E12	USPAT	2	PASTEL, DAVID A/IN

=> s e4 or e5 or e6

```
        19 "PASTAN, IRA"/IN
         9 "PASTAN, IRA H"/IN
         1 "PASTAN, IRA HARRY"/IN
L5      29 "PASTAN, IRA"/IN OR "PASTAN, IRA H"/IN OR "PASTAN, IRA HARR
Y"/
           IN
```

=> s l5 and permut?

```
      7899 PERMUT?
L6       1 L5 AND PERMUT?
```

=> d

1. 5,635,599, Jun. 3, 1997, Fusion proteins comprising circularly **permuted** ligands; **Ira H. Pastan**, et al., 530/351; 435/69.1, 69.5, 69.52, 69.7; 530/350 [IMAGE AVAILABLE]

=> s 5635599 and epo

```
         0 5635599/BI
         0 5,635,599/BI
         0 5635599
           ((5635599 OR 5,635,599)/BI)
      4837 EPO
L7       0 5635599 AND EPO
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=> s 5635599/pn and epo

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         1 5635599/PN
      4837 EPO
L8       0 5635599/PN AND EPO
```

=> s 5635599/pn and erythropoietin

```
         1 5635599/PN
      1324 ERYTHROPOIETIN
L9       1 5635599/PN AND ERYTHROPOIETIN
```

=> d kwic

US PAT NO: **5,635,599** [IMAGE AVAILABLE] L9: 1 of 1

DETDESC:

DETD(8)

A . . . 1 (IL1), interleukin 6 (IL6), interleukin 7 (IL7), granulocyte/macrophage colony-stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF), macrophage colony-stimulating factor (M-CSF), **erythropoietin** and the like. One of skill in the art recognizes that the term growth factor as used herein generally includes. . .

=> bye

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

U.S. Patent & Trademark Office LOGOFF AT 16:02:18 ON 09 OCT 1998

Welcome to DIALOG

Dialog level 98.09.24D

Logon file001 09oct98 15:05:52
? b 411;set files biotech

09oct98 15:06:18 User219511 Session D455.2
$0.00 0.045 DialUnits File410
$0.00 Estimated cost File410
FTSNET 0.005 Hrs.
$0.00 Estimated cost this search
$0.25 Estimated total session cost 0.122 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
(c) 1998 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
You have 48 files in your file list.
(To see banners, use SHOW FILES command)
? s (epo or erythropoietin) and (circul? (5a) permut?)

Your SELECT statement is:
s (epo or erythropoietin) and (circul? (5a) permut?)

Items	File

No files have one or more items; file list includes 48 files.

? s (epo or erythropoietin) and circul? and permut?

Your SELECT statement is:
s (epo or erythropoietin) and circul? and permut?

Items	File
1	5: BIOSIS PREVIEWS(R)_1969-1998/Sep W4
1	34: SciSearch(R) Cited Ref Sci_1990-1998/Oct W1
1	73: EMBASE_1974-1998/Sep W4
1	71: ELSEVIER BIOBASE_1994-1998/Sep W4
1	76: Life Sciences Collection_1982-1998/Aug
1	149: IAC(SM)Health&Wellness DB(SM)_1976-1998/Oct W1
1	155: MEDLINE(R)_1966-1998/Dec W1
1	357: Derwent Biotechnology Abs_1982-1998/Nov B1
1	636: IAC Newsletter DB(TM)_1987-1998/Oct 09

9 files have one or more items; file list includes 48 files.

? save temp; b 155,5,73,257;exs;rd

Temp SearchSave "TD486" stored
09oct98 15:08:34 User219511 Session D455.3
$0.84 0.676 DialUnits File411
$0.84 Estimated cost File411
FTSNET 0.050 Hrs.
$0.84 Estimated cost this search
$1.09 Estimated total session cost 0.798 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-1998/Dec W1
(c) format only 1998 Dialog Corporation
File 5:BIOSIS PREVIEWS(R) 1969-1998/Sep W4
(c) 1998 BIOSIS
*File 5: File is reloaded. Accession number changed.
File 73:EMBASE 1974-1998/Sep W4
(c) 1998 Elsevier Science B.V.
File 257:API EnCompass(TM):News 1975-1998/Oct 09
(c) 1998 Amer. Petroleum Inst.
*File 257: File enhancements, see HELP NEWS 257

Set	Items	Description

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8439 EPO
34174 ERYTHROPOIETIN
1242104 CIRCUL?
3189 PERMUT?
S1 3 (EPO OR ERYTHROPOIETIN) AND CIRCUL? AND PERMUT?
...completed examining records
S2 1 RD (unique items)
? t s2/7/1

2/7/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
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07987126 94350978
Periodicity of DNA bend sites in human epsilon-globin gene region. Possibility of sequence-directed nucleosome phasing.
Wada-Kiyama Y; Kiyama R
Department of Physiology, Nippon Medical School, Tokyo, Japan.
J Biol Chem (UNITED STATES) Sep 2 1994, 269 (35) p22238-44, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Analysis by the %circular% %permutation% assay of the human epsilon-globin gene region revealed that the DNA bend sites were located every 682.5 +/- 132.0 base pairs on average, separating the region into domains. Among 10 major and 1 minor bend sites mapped in the region, the transcription initiation and termination sites of the epsilon-globin gene were located close to the bend sites, and the first and the second exons of the epsilon-globin gene were separated from the third exon by another site. The bend sites were also located anterior to the two Alu family sequences. Short poly(dA).poly(dT) tracts typical for DNA bending were not always present in the sites. Fine mapping of a bend site having no poly(dA).poly(dT) tracts with concatenated oligonucleotides and analysis by S1 nuclease nicking assay indicated that the unusual structure, a base slippage or a partial triplex DNA structure, formed by a polypurine.polypyrimidine sequence in the region is the basis of bending. The bend sites were mapped in the promoter region (within approximately 300 base pairs from the cap site) of the human beta-globin and in c-myc and %erythropoietin% receptor genes, as well as in the mouse beta maj-globin gene. The conservation and the periodicity of the bend sites in the noncoding region suggest the active role of the sites that is a signal for nucleosome phasing.
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09oct98 15:09:19 User219511 Session D455.4
$0.22 0.075 DialUnits File155
$0.20 1 Type(s) in Format 7
$0.20 1 Types
$0.42 Estimated cost File155
$0.51 0.096 DialUnits File5
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OneSearch, 4 files, 0.291 DialUnits FileOS
FTSNET 0.016 Hrs.
$1.79 Estimated cost this search
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